HUMAN FGF-23 GENE AND GENE EXPRESSION PM

Inventor(s): Nobuyuki Itoh et al. Serial No. 09/801,968

vocket No. 201130.40901



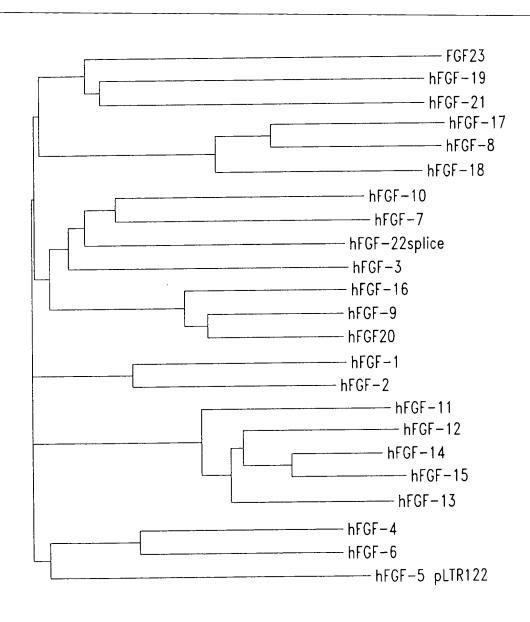


Fig. 1

Title: HUMAN FGF-23 GENE AND GENE EXPRESSION PRODUCTS Inventor(s): Nobuyuk 1 et al. Serial No. 09/801,968

No. 201130.40901

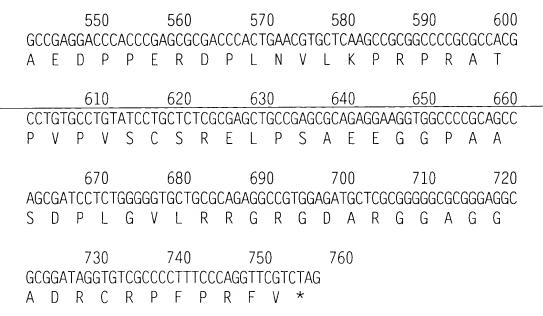
Mouse FGF-23

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ATGCTAGGGACCTGCCTTAGACTCCTGGTGGGCGTGCTCTGCACTGTCTGCAGCTTGGGC M L G T C L R L L V G V L C T V C S L G ACTGCTAGAGCCTATCCAGACACTTCCCCATTGCTTGGCTCCAACTGGGGAAGCCTGACC T A R A Y P D T S P L L G S N W G S L T CACCTGTACACGGCTACAGCCAGGACCAGCTATCACCTACAGATCCATAGGGATGGTCAT H L Y T A T A R T S Y H L O I H R D G H GTAGATGGCACCCCCATCAGACCATCTACAGTGCCCTGATGATTACATCAGAGGACGCC V D G T P H Q T I Y S A L M I T S E D A GGCTCTGTGGTGATAACAGGAGCCATGACTCGAAGGTTCCTTTGTATGGATCTCCACGGC G S V V I T G A M T R R F L C M D L H G AACATTTTTGGATCGCTTCACTTCAGCCCAGAGAATTGCAAGTTCCGCCAGTGGACGCTG NIFGSLHFSPENCKFRQWTL GAGAATGGCTATGACGTCTACTTGTCGCAGAAGCATCACTACCTGGTGAGCCTGGGCCGC ENGYDVYLSOKHHYLVSLGR GCCAAGCGCATTTTCCAGCCGGGCACCAACCCGCCGCCCTTCTCCCAGTTCCTGGCTCGC A K R I F Q P G T N P P P F S Q F L A R AGGAACGAGGTCCCGCTGCTGCACTTCTACACTGTTCGCCCACGGCGCCACACGCGCAGC RNEVPLLHFYTVRPRRHTRS GCCGAGGACCCACCCGAGCGCGACCCACTGAACGTGCTCAAGCCGCGGCCCCGCGCCACG A E D P P E R D P L N V L K P R P R A T

Fig. 2A



Human FGF-23

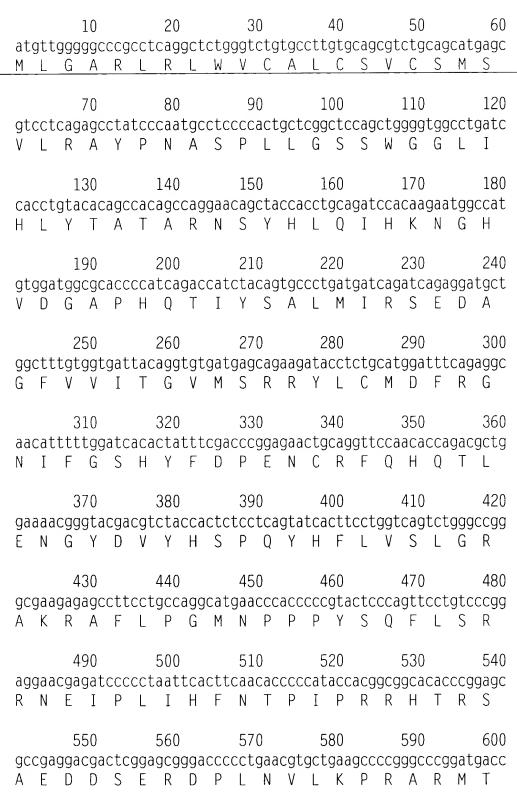


Fig. 3A

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120 VDGTPHQTIYSALMITSEDAGSVVITGAMTRRFLCMDLHGNIFGSLHFSPENCKFRQWTL

120 VDGAPHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPENCRFQHQTL

180 180 ENGYDVYLSQKHHYLVSLGRAKRIFQPGTNPPPFSQFLARRNEVPLLHFYTVRPRRHTRS

240 4EDPPERDPLNVLKPRPRATPVPVSCSRELPSAEEGGPAASDPLGVLRRGRGDARGGAGG ENGYDVYHSPQYHFLVSLGRAKRAFLPGMNPPPYSQFLSRRNEIPLIHFNTPIPRRHTRS ***

240

AEDDSERDPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRVNTHAGGTG

ADRCRPFPRFV 251

**** * PEGCRPFAKFI

251

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216 232 251 RFQHQTLENGYDVYHSPQYHFLVSLGRAK-RAFLPGMNPPPYSQFLSRRNEIPLIHFNTP AFEEE IRPDGYNVYRSEKHRL PVSLSSAKQRQLYKNRGFLPLSHFLPMLPMVPEEPEDLR QIHKNGHVDGAPHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPENC RIRADGVVDCARGQSAHSLLEIKAVALRTVAIKGVHSVRYLCMGADGKMQGLLQYSEEDC IPRRHTRSAEDDSERDPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRV GHLESDMFSSPLETDSMDPFGLVTGLEAVRSPSFEK NTHAGGTGPEGCRPFAKFI

Fig. 5

209

-PGILAPQPPDVGSSDPLSMVGPSQGRSPSYAS

NTHAGGTGPEGCRPFAKFI

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52	09	112	120	172	177	232
<pre>MLGARLRLWVCALCS-VCSMSVLRAYPNASPLLG-SSWGGLIHLYTATARNS-YH</pre>	· > 	LQIHKNGHVDGAPHQTIYSALMIRSEDAGFVVITGVMSRRYLCMDFRGNIFGSHYFDPEN	LEIREDGTVGGAADQSPESLLQLKALKPGVIQILGVKTSRFLCQRPDGALYGSLHFDPEA	CRFQHQTLENGYDVYHSPQYHFLVSLGRAKRAFLPGMNPPPYSQFLSRRNEIPLIHFNTP 172	CSFRELLLEDGYNVYQSEAHGLPLHLPGNKSP-HRDPAPRGPARFLPLPGLPPALPEP 177	IPRRHTRSAEDDSERDPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRV *
Human FGF-23	Human FGF-21					
Human	Human					

Codon usage for yeast (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction
 Gly	GGG	33.00	0.86	0.01
Gly	GGA	70.00	1.82	0.02
Gly	GGT	2672.00	69.62	0.91
Gly	GGC	171.00	4.46	0.06
Glu	GAG	277.00	7.22	0.10
Glu	GAA	2442.00	63.63	0.90
Asp	GAT	1100.00	28.66	0.48
Asp	GAC	1211.00	31.55	0.52
Val	GTG	117.00	3.05	0.04
Val	GTA	75.00	1.95	0.03
Val	GTT	1548.00	40.33	0.56
Val	GTC	1026.00	26.73	0.37
Ala	GCG	36.00	0.94	0.01
Ala	GCA	203.00	5.29	0.06
Ala	GCT	2221.00	57.87	0.65
Ala	GCC	969.00	25.25	0.28
Arg	AGG	20.00	0.52	0.01
Arg	AGA	1336.00	34.81	0.83
Ser	AGT	116.00	3.02	0.05
Ser	AGC	94.00	2.45	0.04
Lys	AAG	2365.00	61.62	0.78
Lys	AAA	651.00	16.96	0.22
Asn	AAT	347.00	9.04	0.22
Asn	AAC	1259.00	32.80	0.78
Met	ATG	766.00	19.96	1.00
Ile	ATA	43.00	1.12	0.02
Ile	ATT	1223.00	31.87	0.52
Ile	ATC	1070.00	27.88	0.46
Thr	ACG	28.00	0.73	0.01
Thr	ACA	126.00	3.28	0.06

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Fig. 7A

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Thr **ACT** 1129.00 29.42 0.50 Thr ACC 962.00 25.07 0.43 TGG 325.00 8.47 1.00 Trp 10.00 0.26 End TGA 0.09 254.00 Cys TGT 6.62 0.89 33.00 Cys TGC 0.86 0.11 0.10 End 0.29 TAG 11.00 End TAA 85.00 2.21 0.80 Tyr 219.00 5.71 TAT 0.19 23.79 Tyr TAC 913.00 0.81 57.38 TTG 2202.00 0.69 Leu 0.18 THE REAL PLANTS AND THE PARTY OF THE PARTY O Leu TTA 576.00 15.01 11.26 Phe TTT 432.00 0.27 TTC 1145.00 29.83 0.73 Phe Ser TCG 26.00 0.68 0.01 149.00 3.88 Ser TCA 0.06 Ō, TCT 33.33 0.52 Ser 1279.00 an Hill The TCC 21.31 Ser 818.00 0.33 CGG 0.00 Arg 0.00 0.00 CGA 0.03 Arg 1.00 0.00 CGT Arg 249.00 6.49 0.15 5.00 0.13 0.00 CGC Arg Gln CAG 62.00 0.05 1.62 Gln CAA 1225.00 31.92 0.95 CAT 6.15 His 236.00 0.35 His CAC 433.00 11.28 0.65 CTG 52.00 Leu 1.35 0.02 236.00 Leu CTA 6.15 0.07 CTT 90.00 2.35 0.03 Leu CTC Leu 14.00 0.36 0.00 CCG Pro 10.00 0.26 0.01 Pro CCA 1271.00 33.12 0.80 279.00 Pro CCT7.27 0.18 CCC Pro 33.00 0.86 0.02

Inventor(s): Nobuyu

Fig. 7B

Inventor(s): Nobuyu

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Codon usage for Drosophila (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction
Gly Gly	GGG GGA	6.00 380.00	0.28	0.00
Gly Gly	GGT GGC	575.00 746.00	27.29 35.41	0.34
Glu	GAG	1217.00	57.77	0.91
Glu	GAA	115.00	5.46	0.09
Asp	GAT	503.00	23.88	0.43
Asp	GAC	654.00	31.04	0.57
Val Val Val	GTG GTA GTT GTC	719.00 29.00 226.00 608.00	34.13 1.38 10.73 28.86	0.45 0.02 0.14 0.38
Ala	GCG	94.00	4.46	0.05
Ala	GCA	80.00	3.80	0.04
Ala	GCT	446.00	21.17	0.24
Ala	GCC	1277.00	60.61	0.67
Arg	AGG	48.00	2.28	0.06
Arg	AGA	12.00	0.57	0.01
Ser	AGT	16.00	0.76	0.01
Ser	AGC	267.00	12.67	0.23
Lys	AAG	1360.00	64.55	0.93
Lys	AAA	108.00	5.13	0.07
Asn	AAT	127.00	6.03	0.13
Asn	AAC	878.00	41.67	0.87
Met	ATG	387.00	18.37	1.00
Ile	ATA	4.00	0.19	0.00
Ile	ATT	390.00	18.51	0.29
Ile	ATC	969.00	45.99	0.71
Thr	ACG	114.00	5.41	0.08
Thr	ACA	34.00	1.61	0.02

Fig. 8A

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	Thr Thr	ACT ACC	164.00 1127.00	7.78 53.49	0.11 0.78	
	Trp End Cys Cys	TGG TGA TGT TGC	243.00 1.00 20.00 220.00	11.53 0.05 0.95 10.44	1.00 0.01 0.08 0.92	
	End End Tyr Tyr	TAG TAA TAT TAC	12.00 58.00 113.00 574.00	0.57 2.75 5.36 27.25	0.17 0.82 0.16 0.84	
րում հայ գրու Մուլ հայ գրու մում Մուլ հայ գրու հ	Leu Leu Phe Phe	TTG TTA TTT TTC	210.00 9.00 62.00 635.00	9.97 0.43 2.94 30.14	0.12 0.01 0.09 0.91	
H (C)	Ser Ser Ser Ser	TCG TCA TCT TCC	195.00 29.00 103.00 558.00	9.26 1.38 4.89 26.49	0.17 0.02 0.09 0.48	
reng, errig gener errig gene ett. Haalt ge ^{er} Mad Mass had ooks	Arg Arg Arg Arg	CGG CGA CGT CGC	7.00 25.00 281.00 465.00	0.33 1.19 13.34 22.07	0.01 0.03 0.34 0.55	
	Gln Gln His His	CAG CAA CAT CAC	703.00 66.00 88.00 312.00	33.37 3.13 4.18 14.81	0.91 0.09 0.22 0.78	
	Leu Leu Leu Leu	CTG CTA CTT CTC	1182.00 21.00 55.00 224.00	56.10 1.00 2.61 10.63	0.69 0.01 0.03 0.13	
	Pro Pro Pro Pro	CCG CCA CCT CCC	84.00 135.00 72.00 626.00	3.99 6.41 3.42 29.71	0.09 0.15 0.08 0.68	
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h et al.

Inventor(s): Nobuyuk

Fig. 8B

Inventor(s): Nobuyuk h et al.

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No. 201130.40901

Codon usage for enteric bacterial (highly expressed) genes

AmAcid	Codon	Number	/1000	Fraction
Gly Gly	GGG GGA	13.00	1.89	0.02
Gly	GGC	365.00	52.99	0.59
Gly		238.00	34.55	0.38
Glu	GAG	108.00	15.68	0.22
Glu	GAA	394.00	57.20	0.78
Asp	GAU	149.00	21.63	0.33
Asp	GAC	298.00	43.26	0.67
Val Val Val	GUG GUA GUU GUC	93.00 146.00 289.00 38.00	13.50 21.20 41.96 5.52	0.16 0.26 0.51 0.07
Ala	GCG	161.00	23.37	0.26
Ala	GCA	173.00	25.12	0.28
Ala	GCU	212.00	30.78	0.35
Ala	GCC	62.00	9.00	0.10
Arg	AGG	1.00	0.15	0.00
Arg	AGA	0.00	0.00	0.00
Ser	AGU	9.00	1.31	0.03
Ser	AGC	71.00	10.31	0.20
Lys	AAG	111.00	16.11	0.26
Lys	AAA	320.00	46.46	0.74
Asn	AAU	19.00	2.76	0.06
Asn	AAC	274.00	39.78	0.94
Met	AUG	170.00	24.68	1.00
Ile	AUA	1.00	0.15	0.00
Ile	AUU	70.00	10.16	0.17
Ile	AUC	345.00	50.09	0.83
Thr	ACG	25.00	3.63	0.07
Thr	ACA	14.00	2.03	0.04

Fig. 9A

	Inventor(s): Nobuyuk	_	-23 GENE AND G Serial No	. 09/801,968		No. 201130.40901
	Thr	ACU	130.00	18.87	0.35	
	Thr	ACC	206.00	29.91	0.55	
	Trp	UGG	55.00	7.98	1.00	
	End	UGA	0.00	0.00	0.00	
	Cys	UGU	22.00	3.19	0.49	
	Cys	UGC	23.00	3.34	0.51	
	End	UAG	0.00	0.00	0.00	
	End	UAA	0.00	0.00	0.00	
	Tyr	UAU	51.00	7.40	0.24	
	Tyr	UAC	157.00	22.79	0.75	
	Leu	UUG	18.00	2.61	0.03	
	Leu	UUA	12.00	1.74	0.02	
75 13 17 15	Phe	UUU	51.00	7.40	0.24	
20 12 12 12 12 12 12 12 12 12 12 12 12 12	Phe	UUC	166.00	24.10	0.76	
E.S. M. The Erry C.S. (The Error Error Error) and the Error Error Error Error Error Error Error Error Error Er	Ser	UCG	14.00	2.03	0.04	
	Ser	UCA	7.00	1.02	0.02	
	Ser	UCU	120.00	17.42	0.34	
72 13 mm	Ser	UCC	131.00	19.02	0.37	
From the Company of the State	Arg	CGG	1.00	0.15	0.00	
	Arg	CGA	2.00	0.29	0.01	
1. j.	Arg	CGU	290.00	42.10	0.74	
	Arg	CGC	96.00	13.94	0.25	
	Gln	CAG	233.00	33.83	0.86	
	Gln	CAA	37.00	5.37	0.14	
	His	CAU	18.00	2.61	0.17	
	His	CAC	85.00	12.34	0.83	
	Leu	CUG	480.00	69.69	0.83	
	Leu	CUA	2.00	0.29	0.00	
	Leu	CUU	25.00	3.63	0.04	
	Leu	CUC	38.00	5.52	0.07	
	Pro	CCG	190.00	27.58	0.77	
	Pro	CCA	36.00	5.23	0.15	
	Pro	CCU	19.00	2.76	0.08	
	Pro	CCC	1.00	0.15	0.00	
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Fig. 9B

Inventor(s): Nobuyuk h et al. Serial No. 09/801

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l. Serial No. 09/801,968 No. 201130.40901

Chromosomal localization of genes of the FGF family in human

Gene	Localization	Gene	Localization
FGF-1 FGF-2 FGF-3 FGF-4 FGF-5 FGF-6 FGF-7 FGF-8 FGF-9 FGF-10 FGF-11	5q31.3-q33.2 4q26 11q13 11q13.3 4q21 12p13 15q13-q22 10q25-q26 13q11-q12 5p12-p13	FGF-12 FGF-13 FGF-14 (FGF-15) FGF-16 FGF-17 FGF-18 FGF-20 FGF-21 FGF-21 FGF-21	3q29-qter X 13 - 8p21 5 11q13.1 8p21.3-p22 19q13.1-qter 19p13.3 12p13

Human FGF-15 gene has not been identified. The localization of human FGF-16 gene has not been determined.

Fig. 10

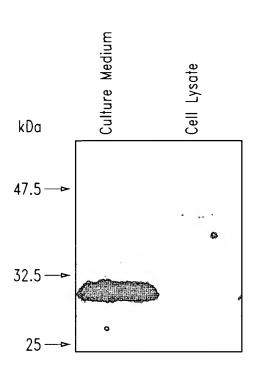


Fig. 11

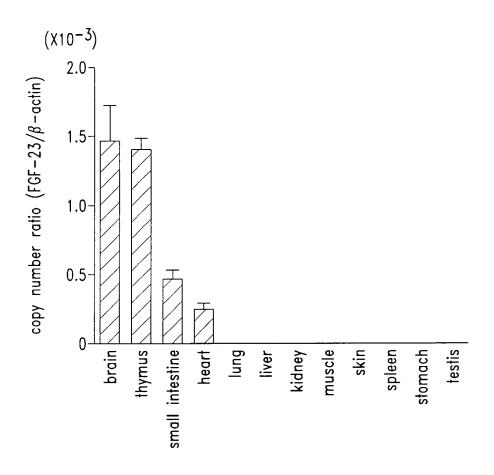


Fig. 12



Fig. 13A

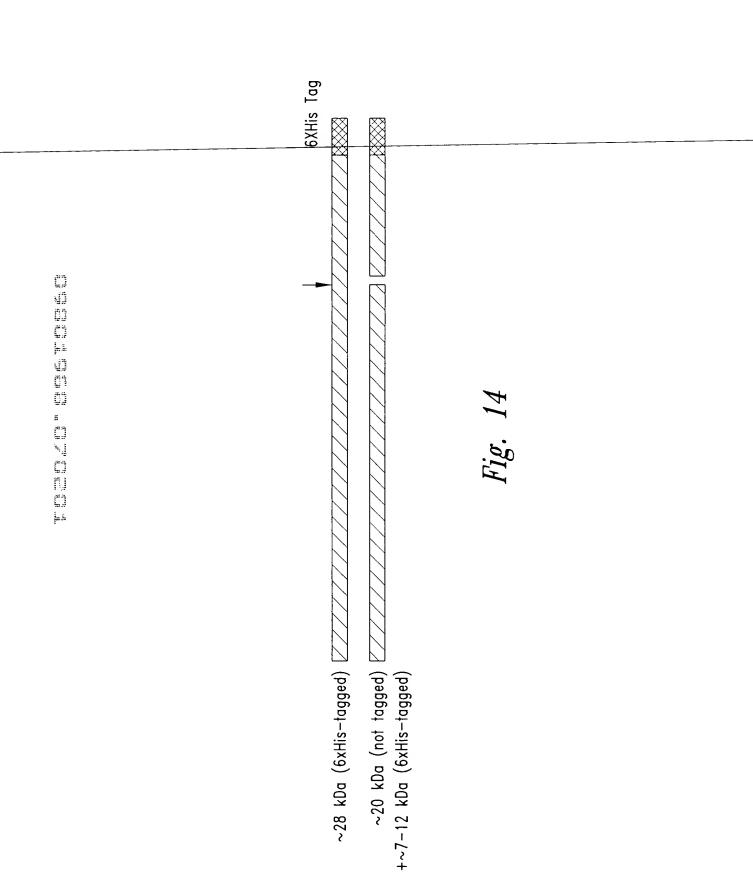


Fig. 13B

Title: HUMAN FGF-23 GENE AND GENE EXPRESSION PRODUCTS Inventor(s): Nobuyuk h et al.

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Title: HUMAN FGF-23 GENE AND GENE EXPRESSION PRODUCTS No. 201130.40901 Inventor(s): Nobuyuk h et al. Serial No. 09/801,968

			11774	kDa	-9713	-	₁ 7520 kDa
		(213)	213 220		$230 \mid kDa$	240	250
	FGF23	(141)	AKRAFLPGMNP	PPYSQI	FLSRRNEIPI	_ [HFNTPIPRF	RHTRSAEDDSER
	hFGF-1	(121)	NWFVGLKKNGS				
	hFGF-10	(175)	QMYVALINGKGA	PRRGQ	KTRRKNTS	SAHFLAMVVHS)
	hFGF-11	(170)	AWYLGLDREGO	, ,		1 1 1	
	hFGF-12	(172)	AWFLGLNKEGQ	IMKGN		SHFVPKPIEV	/CMYR
	hFGF-13	(168)	GWYLGLNKEGE				
	hFGF-14	(170)	AWFLGLNKEGQ	AMKGN:	RYKKTKPA	\ АНFLРҚРЦЕ\	/AMYR
- 44 - 71	hFGF-15	(175)	AWFLGLNKEGQ				
	hFGF-16	(160)	QYYVALINKDGS				
	hFGF-17	(149)	-WFMAFTROGR	PROAS	RSRQNQRI	AHF IKRLYQG	QLPFPNHAEK-
		(149)					GQPEL
ŌÌ	hFGF-19	(141)					/PEEPE-
a Fig	hFGF-2	(123)	-WYVALKRTGQ				
	hFGF-21	(143)	-LPLHLPGNKS				
=3	hFGF-3	(152)	LWYVSVNGKGR	<u>P</u> RRĢF	KTRRTQKS	SUFLPRVUDH	IRDHEMVRQLQ-
	hFGF-4	(177)	-MFIALSKNGK				
	•	(187)	EWYVALNKRGK				
2	hFGF-6	(179)	-TYIALSKYGR				
	hFGF-7	(162)	EMFVALINQKQI				
	hFGF-8	(167)	-WYMAFTRKGR				
	hFGF-9	(161)	RYYVALINKOGT	PRĒĠT.	RTKRHQKF	THFLPRPVDP	PDKVP
	hFGF-20	(164)	RYFVALNKOGT	PROGA:	RSKRHQKF	THFLPRHYDR	PERVP
	hFGF-22Nobu	(139)	-MFLAUDRRGG	PRPGG.	{RTRRYHLS	AHFLPVLVS-	
	Consensus	(213)	WYVAL K G F	PRKG	RTKK	AHFLPR V	

Fig. 15A

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6630 kDa 280 300 310 260 270 290 DPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRVNTHAGGTGPEGCRPFAKFI EPSLHSVPEAS-----P--SSPPAP-------EPSLHEIGE---KQGR-S--RKSSGTPTMNGGKVVNQDST--------EPSLHDLTEFS-RSGSGTPTKSRSVSGVLNGGKSMSHNEST--------EPSLHDVGETVPKPGV-TPSKSTSASAIMNGGKPVNKSKTT------EPSLHDVGETVPKPGV-TPSKSTSASAIMNGGKPVNKSKTT---------SMSRDLFHYR-----QKQFEFVGSAPTRRTKRTRR----PQPLT-------QKPFKYTTVTKRSRRIRPTH----PA-------DLRGHLESDMFSSPLETDSMDPFGLVTGLEAVRSPSFEK-----EPPGILAPQPP-DVGSSDPLSMVGPSQGRSPSYAS------SGLPRPPGKGVQPRRRRQKQSPDNLEPSHVQASRLGSQLEASAH------PEKKKPPSPIKPKIPLSAPRKNTNSVKYRLKFRFG------SLRFEFLNYPPFTRSLRGSQRTWAPEPR------ELYKDILSOS------

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Fig. 15B



Cleavage of baculovirus-expressed

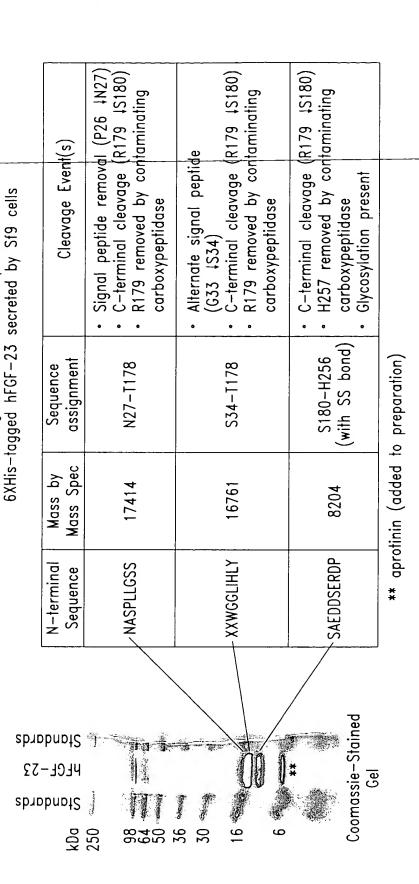


Fig. 16